SUPPORT FOR THE AMENDMENTS

Newly-added Claims 109-149 are supported by the specification and the original claims. Accordingly, no new matter is believed to have been added to the present application by the amendments submitted above.

REMARKS

Claims 109-149 are pending. Favorable reconsideration is respectfully requested.

The present invention relates to a method of determining the initial amounts of individual species of a target gene, comprising:

amplifying a target gene and monitoring the amplification by real-time PCR;

performing a polymorphous analysis selected from the group consisting of T-RELP (terminal restriction fragment length polymorphism), RFLP (restriction fragment length polymorphism), SSCP (single strand conformation) or CFLP (cleavage fragment length polymorphism) with respect to the amplified target gene to determine a polymorphous composition ratio of individual species of the target gene; and

determining the initial amount of the target gene; and

determining the initial amounts of individual species of the target gene.

See Claim 109.

The present invention also relates to a method of determining the initial amounts of individual species of a target gene, comprising:

amplifying a target gene and monitoring the amplification by real-time PCR;

performing a polymorphous analysis with respect to the amplified target gene to determine a polymorphous composition ratio of individual species of the target gene; and

determining the initial amount of the target gene; and

determining the initial amounts of individual species of the target gene,

wherein the real-time PCR is accomplished with a nucleic acid probe,

wherein the probe comprises a single-stranded oligonucleotide capable of hybridizing to the target nucleic gene,

wherein the probe is labeled with a fluorescent dye and a quencher substance,

wherein the oligonucleotide is labeled with the fluorescent dye and the quencher substance such that the intensity of fluorescence in a hybridization reaction system increases when the probe is hybridized with the target gene, and

wherein the oligonucleotide forms no stem-loop structure between bases at positions where the oligonucleotide is labeled with the fluorescent dye and the quencher substance.. See Claim 110.

The present invention also relates to a method for determining the initial amounts of individual species of a target gene, comprising:

(1) amplifying a target gene and monitoring the amplification by a quantitative real-time PCR making use of a fluorescence-quenching probe labeled with a fluorescent dye at the 5'-end thereof as a primer(s);

(2) digesting the amplified target gene using an endonuclease;

(3) the obtained gene fragments is thermally modified into single-stranded forms

(4) detecting gene fragment(s) labeled with a fluorescent dye at the 5'-end thereof by a sequencer or HPLC by measuring a fluorescent emission in the fluorescent dye as a signaling marker;

(5) measuring the fluorescent intensity of fragment peaks detected by the sequencer or HPLC, which peaks are caused by the gene fragments,

and then, determining a composition ratio of individual fragments; and

(6) determining the initial amount of the target gene; and

(7) determining the initial amounts of individual species of the target gene,

wherein said fluorescence-quenching probe is labeled at a phosphate group or a 5'-OH group of a ribose or deoxyribose which is obtained by dephosphorization of the 5'-end, and has a base sequence designed such that, when the probe hybridizes at the end portion thereof to the target nucleic acid, at least one G (guanine) base exists in a base sequence of

the target gene at a portion 1 to 3 bases apart from end base of the target gene hybridized with the probe.

See Claim 143.

The rejection of the claims under 35 U.S.C. §102(e) over Kurane et al. (U.S. patent No. 6,699,661) is respectfully traversed.

Newly-added independent Claim 109 corresponds to Claim 95 re-written in independent form. Newly-added Claim 110 corresponds to Claim 83 re-written in independent form.

Neither Claim 95 nor Claim 83 was rejected under 35 U.S.C. §102(e) over Kurane et al. See the Office Action dated February 8, 2006 at page 5, bottom. Accordingly, the rejection does not apply to the newly-added claims. In addition, the reference fails to describe steps (2)-(5) of Claim 143.

Therefore, withdrawal of this ground of rejection is respectfully requested.

The rejections of Claims 83 and 95 under 35 U.S.C. §103(a) over Kurane et al. alone or in combination with Reed et al. (U.S. patent No. 6,727,356) are respectfully traversed. The cited references fail to suggest the claimed methods.

The present invention relates to a method of determining the initial amounts of individual species of a target gene, i.e., determining the initial amounts of plural polymorphous genes.

Kurane et al. fails to suggest the claimed method, in particular each of the steps in Claims 109, the method as specified in Claim 110, and steps (2)-(5) specified in Claim 143. In fact, the reference relates to SNP type polymorphisms but is not related to a polymorphous analysis method for analyzing and determining the initial amounts of plural polymorphous genes. Accordingly, withdrawal of this ground of rejection is respectfully requested.

The rejection of the claims under 35 U.S.C. §112, second paragraph, is believed to be obviated by the amendment submitted above. The preambles of the independent claims have been appropriately amended.

In view of the foregoing, the claims are definite within the meaning of 35 U.S.C. §112, second paragraph. Withdrawal of this ground of rejection is respectfully requested.

The Restriction Requirement is believed to be moot. The non-elected subject matter has been removed from the claims.

Applicants submit that the present application is in condition for allowance. Early notice to this effect is earnestly solicited.

Respectfully submitted,

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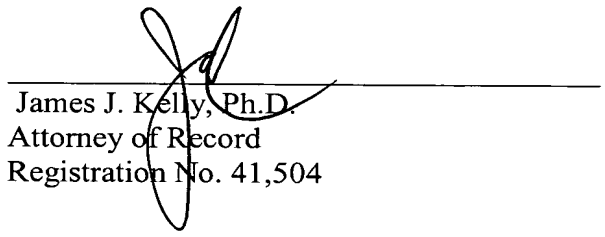

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